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INSTABILITY IN HUMAN FOREARM MOVEMENTS STUDIED WITH FEED-BACK-CONTROLLED ELECTRICAL STIMULATION OF MUSCLES

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SUMMARY

1. Amplitude-modulated electrical stimulation was applied to the elbow flexors and extensors to produce movements of the forearm in normal subjects. The parameters of the modulating (command) signal were set in isometric trials so as to produce equal and opposite background torques, and equal and supportive torque modulations.

2. Bode plots relating forearm movement to command signal (modulating) frequency showed the muscle–load to have a low-pass characteristic similar to that previously described in the cat, and a slightly larger bandwidth than described previously in man.

3. The transduced forearm signals were fed back to provide the command signal to the stimulators via a filter which mimicked the transfer function of muscle spindle primary endings. In effect this replaced the neural part of the reflex arc with an accessible model, but left the muscle–load effector intact.

4. All six subjects developed forearm oscillations (tremor) when the loop gain exceeded a threshold value. The mean tremor frequency at onset was 4·4 Hz, which was similar to that of the equivalent vibration-evoked tremor (previous paper, Prochazka & Trend, 1988).

5. With the linear spindle model, oscillations tended to grow rapidly in amplitude, and the stimuli became painful. The inclusion of a logarithmic limiting element resulted in stable oscillations, without significant alterations in frequency. This allowed us to study the effect on tremor of including analog delays in the loop, mimicking those associated with peripheral nerve transmission and central reflexes. In one subject, loop delays of 0, 20, 40 and 100 ms resulted in tremor at 4·0, 3·6, 3·0 and 2·1 Hz respectively, as quantified by spectral analysis.

6. By considering separately the phase contributions of the different elements of the reflex arc, including delays, it became clear that muscle–load properties were important in setting the upper limit of tremor frequencies which could conceivably be supported by reflexes.

7. The results support the conclusion of the related vibration study (Prochazka & Trend, 1988), that for moderate levels of background co-contraction, the contribution

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of stretch reflexes to tremor at the elbow should be sought in the 3–5 Hz range. Exaggerated long-latency reflexes would be expected to reduce these baseline frequencies by 1 or 2 Hz.

INTRODUCTION

In the previous paper we concluded that stretch reflexes acting about the human elbow joint would evoke variations in muscle force timed in such a way as to assist tremor in the 3–8 Hz range. The purpose of the present paper is to further examine transmission in the different elements of the reflex arc, and to assess the effect of alterations in the central reflex delay.

The first step in analysing the stability criteria of a feed-back-control system is usually to establish the transfer function around the (open) loop. If possible, each of the elements in the pathway is characterized separately, because it is often useful to know which of them contribute the major phase shifts affecting stability. Partridge (1965, 1966) was the first to attempt a thorough analysis of the frequency response of load-moving mammalian muscle stimulated via its nerve supply. Corresponding analyses of the main sensory feed-back elements of the reflex arc, the muscle spindle afferents, commenced with the work of Poppele & Terzuolo (1968) and Matthews & Stein (1968, 1969). Poppele & Terzuolo (1968) found that the phase advances in spindle primary endings matched nearly exactly the phase lags of isometric muscle force on neural input and so in theory the net phase shift in the afferent and efferent limbs of the reflex arc should be close to zero. Indeed when Rosenthal, McKean, Roberts & Terzuolo (1970) performed a frequency analysis of the stretch reflex in the decerebrate cat, they found that reflex force showed a small (20–30 deg), fairly constant phase advance on imposed stretch over the whole physiological range of frequencies. The fact that the dynamics of the reflex arc were apparently determined solely by its peripheral elements suggested, rather surprisingly, that transmission through the CNS occurred without any significant dynamic modification. This was more directly supported by the observation that the firing rates of motoneurones activated reflexly by stretching had virtually identical frequency–response curves to those of spindle primary endings.

These results in cat established the basic dynamic characteristics of the elements in the reflex arc, but for various reasons they do not provide enough information to allow accurate predictions to be made about the behaviour of stretch reflexes acting about particular joints in humans. First, by describing the output of the reflex arc in terms of isometric force, Rosenthal *et al.* (1970) omitted the non-linear dynamics of load-moving muscle (Partridge, 1966). There are no simple transfer functions relating displacement of a load to isometric muscle force and so the description of the loop is incomplete. This in turn precludes any meaningful attempt at deriving stability criteria. Second, even with the inclusion of load-moving properties, the mechanical and neuromuscular parameters relevant to a particular joint are in general inaccessible in human subjects. Third, the transfer characteristics of reflexes in decerebrate cats might differ significantly from those in awake human subjects.

Previously, we studied the way in which stretch reflexes moved the forearm when signals were artificially injected into the afferent pathway (Prochazka & Trend, 1988). Because of the uncertainties regarding the 'taking over' of afferent firing, we

felt that a useful complementary experiment could be performed which would bypass more of the reflex arc, and also allow the load-moving properties of the peripheral 'neuromuscular effector' to be isolated. Our approach was to stimulate the elbow flexor and extensor muscles electrically with amplitude-modulated pulse trains applied percutaneously at the motor points. As in the vibration experiments, open- and closed-loop trials were performed. The results confirmed that at low levels of co-contraction, short-latency stretch reflexes would be expected to contribute to forearm tremors of unexpectedly low frequencies (3–4 Hz). The inclusion of delays mimicking long-loop conduction in the reflex arc reduced these frequencies in a predictable way. A preliminary report of these findings has appeared (Jacks, Prochazka & Trend, 1986).

METHODS

Six normal adult subjects were studied in detail, three on several different occasions. The experiments were performed with the understanding and consent of each subject. A typical experiment lasted 2 h. As in the related vibration study (Prochazka & Trend, 1988), the subject was seated comfortably and the right shoulder was supported against a vertical bar (Fig. 1). The right upper limb was abducted 90 deg at the shoulder. The forearm was firmly strapped to a horizontal arm rest in a position mid-way between pronation and supination, with the hand strapped to a vertical rod. The arm rest was pivoted at the elbow, allowing pure flexion and extension movements about the joint. Two electrodes, each consisting of a rectangle (50 × 30 mm) of conductive rubber sheet (Primasil Ltd U.K.) and a thin (2 mm) layer of damp kitchen sponge, were strapped firmly over the motor points of biceps and triceps brachii (Fig. 1). A similar reference electrode was strapped to the anterior of the leg, just distal to the knee after the method of Vodovnik, Crochetiere & Reswick (1967).

In the relaxed subject, forearm flexion and extension could then be generated by applying amplitude-modulated trains of electrical impulses through these electrodes (30 s^{-1}, biphasic pulses, first phase rectangular 80–120 mA, 100 μs; second phase exponential, peak 16–24 mA, time constant 0·5 ms). Initially, some of the subjects intervened voluntarily, either assisting or resisting the electrically evoked movements. This was readily detectable as an irregularity in the relationship between stimulus and response waveforms. After a little practice, all subjects were able to relax their muscles and eliminate any element of voluntary contribution. Under these conditions, we feel it most unlikely that the inevitable activation of skin and muscle afferents by the electrical stimuli could elicit reflex contributions to the movements. The reproducibility of the contractions, and the linearity of the relationship between stimulus amplitude and isometric force, also depended critically upon electrode placement. Optimal electrode positioning was achieved by trial and error for flexion and extension separately, using sinusoidally modulated pulse trains, and with reference to the resulting isometric force monitored at the wrist (measured using a low-compliance (*ca.* 20 μm/N) force transducer consisting of two Kulite UHP 5000-060 bonded to a U-shaped former, resistance variations being detected by a bridge circuit and displayed on a Tektronix 5111 oscilloscope). Figure 2 shows the time course of isometric extensor and flexor torques in response to separate trains of amplitude-modulated impulses. The envelopes of the peak voltages of the impulses are shown in this Figure (in separate measurements peak voltages showed a near-linear relationship with the (rectangular) current amplitude). The aim was to produce sinusoidal fluctuations of equal amplitude in flexor and extensor torque, superimposed upon background torques corresponding to a 10% maximal voluntary co-contraction. The depth of stimulus amplitude modulation to achieve this was generally different for the flexors and extensors, as typified by the stimulus envelopes of Fig. 2. The modulating signal was routed through separate amplifiers whose gains were set to produce flexor and extensor torques of equal modulation depth and whose offsets were set to produce 10% of the maximal voluntary torques. These settings were then held constant for all subsequent trials. One of the amplifiers inverted the modulating signal so that for simultaneous flexor and extensor stimulation, deviations of the command signal which produced an increase in extensor torque produced an equal reduction in flexor torque (Fig. 1).

Initially the flexor and extensor stimulus spikes were generated synchronously. However, this

was found to result in cross-talk, in that responses of one muscle group were influenced by the stimuli to the antagonists. This problem was overcome by interleaving the stimulus trains (flexor and extensor spikes being timed to occur alternately at 17 ms intervals). Independent activation of the agonists and antagonists then became possible, as judged by the responses to separate modulation of the two pulse trains.

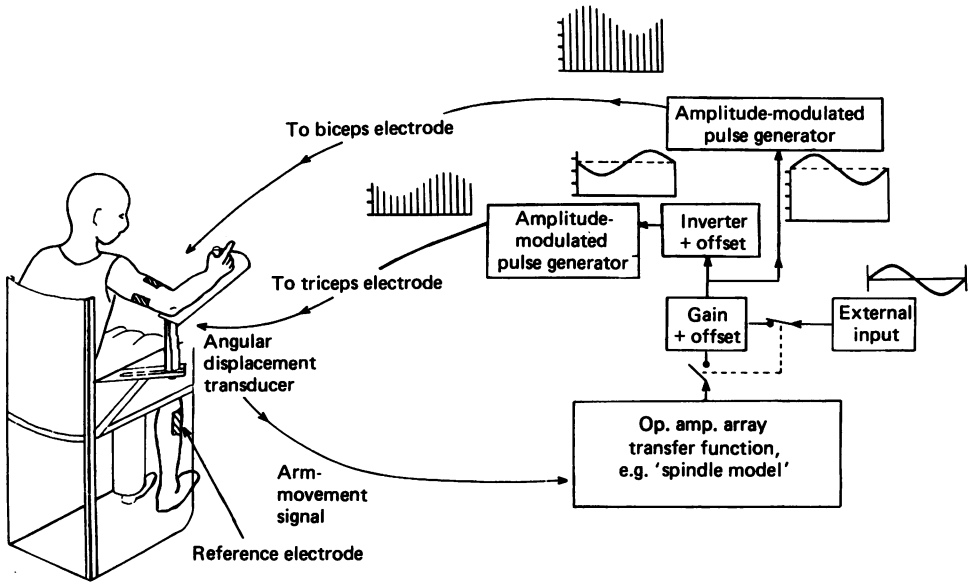

Fig. 1. Experimental arrangement. The subject's elbow flexors and extensors were independently stimulated through conductive rubber electrodes strapped to the arm, the indifferent electrode being sited on the leg. Stimulus pulses were amplitude modulated, either in open-loop mode via the external input or closed-loop mode via the spindle model: operational amplifier array. The transfer function used was that of Poppele & Bowman (1970):

$$\frac{K(s+0{\cdot}44)(s+11{\cdot}3)(s+44)}{(s+0{\cdot}816)}.$$

Angular displacement of the elbow was measured using a sensitive cantilever transducer (Kulite UHP 5000-060 semiconductor strain gauge bonded to a 4 mm beryllium copper strip), one end of which was attached to the moving arm rest, the other end being deflected by a lubricated Teflon post fixed to the vertical support. With the stimulus parameters set as in Fig. 2 and the arm free to move, the displacement responses could now be recorded in both open- and closed-loop modes.

In open-loop mode the modulating signal (derived from a function generator: 'external input' in Fig. 1) directly drove the amplitude-modulated pulse generators to produce forearm movements. The modulating signal and the resulting forearm displacement or torque were sampled and displayed with the use of a BBC microcomputer linked to a Unilab interface (O'Brien, Prochazka & Vincent, 1985). Records of single trials or averages of several trials were printed out with an Epson FX-80 dot-matrix printer, or stored on magnetic disc (Acorn DFS) for later analysis. Bode plots were constructed showing the amplitude and phase of the displacement response to the modulating signal at different frequencies in the range 0·5–12 Hz.

In closed-loop mode the forearm displacement signal was fed back through an electronic filter which closely mimicked the transducing properties of muscle spindle Ia afferents in the linear range (Poppele & Bowman, 1970; Poppele & Kennedy, 1974). The transfer function used was discussed in detail in the previous paper. A simple potentiometric adjustment ('Gain+offset' in Fig. 1) allowed the gain of the spindle model to be altered, without altering the dynamics of the transfer

function. The filtered displacement signal and its inverse modulated the outputs of the pulse generators. As in the vibration experiments (Prochazka & Trend, 1988), instability occurred at some point as the loop gain was progressively increased. The tremor was spectrally analysed with the use of a laboratory interface (Cambridge Electronic Design 1401) operating a Fast Fourier Transform algorithm. Delays mimicking those due to conduction in the reflex arc and in polysnaptic CNS pathways were introduced into the closed loop with the use of an analog delay line. The changes in tremor frequency resulting from these delays were also quantified with spectral analysis.

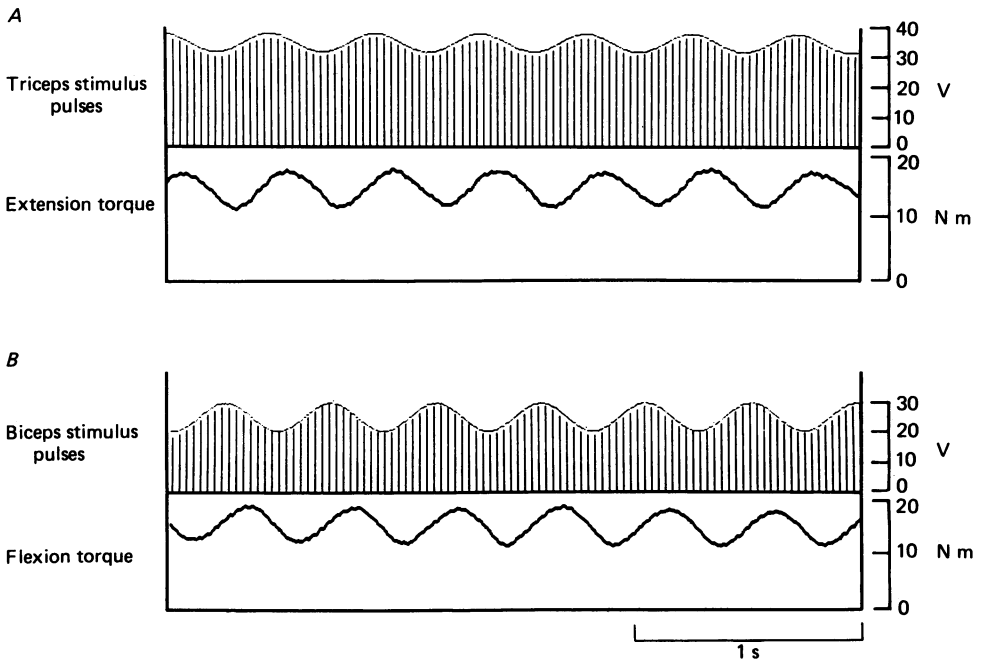

Fig. 2. Isometric torques (monitored by a force gauge attached to a wristlet) in response to amplitude-modulated stimulus pulses. *A* and *B*, separate trials, triceps and biceps respectively. Only the envelope of the stimulus pulses was recorded, the vertical hatching, representing the pulses, being added graphically. Note that the offset and modulation depth of the two stimulus envelopes were independently set so as to produce matching flexor and extensor torques, and equal and opposite mean levels corresponding to 10% co-contraction.

RESULTS

Open-loop trials

As mentioned above, there are no simple transfer functions relating isometric muscle force to isotonic displacement of inertial loads. However, the frequency–response curves of isometric force elicited by electrical stimulation of isolated cat muscles are well established, and provide a useful description of the basic force-generating mechanism (Partridge, 1965; Poppele & Terzuolo, 1968; Rosenthal *et al.* 1970). We performed similar analyses of the isometric responses of the elbow flexors and extensors in our subjects. Figure 3 shows representative Bode plots obtained in one subject of extensor and flexor torques at different command signal frequencies ranging from 1 to 10 Hz. Amplitude and phase measurements were made on

averaged records of sixteen or thirty-two response cycles. The characteristics were similar for the two muscle groups, and showed low-pass properties in line with cat gastrocnemius, soleus (Rosenthal *et al.* 1970) and plantaris muscles (Mannard &

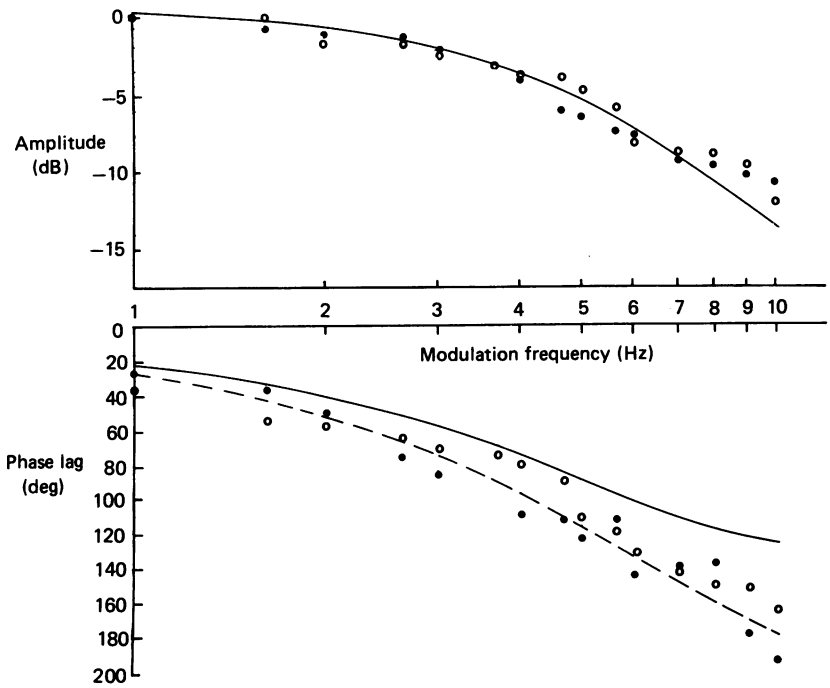

Fig. 3. Amplitude and phase plots of torque *vs.* stimulus modulation frequency in one subject. ○, extensor torque; ●, flexor torque. The continuous curves give the responses expected of a linear, critically damped second-order system with a natural frequency of 5·0 Hz. The dashed curve shows the phase expected after the addition of lags due to a delay of 15 ms (see text).

Stein, 1973: note erratum substituting plantaris for soleus). On fitting the gain curve of a critically damped second-order system to our data, we found the roll-off frequency for the best match to be 5·0 Hz (Fig. 3). This was identical to the cat data (Mannard & Stein, 1973). When the phase lags due to an assumed 15 ms propagation and excitation–contraction delay were added to the phase curve of the second-order system, the resultant curve fitted the data remarkably well (Fig. 3, lower panel, dashed curve). Isometric force lagged the command signal by 180 deg at 9–10 Hz in our subject compared with 15 Hz in the cat (Mannard & Stein, 1973). The frequency (which we shall call f_{180}) at which there is a 180 deg phase lag around a feed-back loop has a special significance, in that when the loop is closed and the gain is sufficiently high, instability results, and oscillations develop at this frequency.

Our results are also comparable to those of Aaron & Stein (1976) who used intramuscular, randomized stimulation of human biceps, and derived amplitude and phase plots by spectrally analysing the isometric force responses. A fitted second-order function in that case indicated a roll-off at 2·3 Hz and f_{180} of 6·3 Hz. The somewhat lower values in Aaron & Stein's study might have been due to incomplete

muscle activation by the intramuscular needle electrodes used, and a stimulus time course which allowed periods of zero tension.

The next step was to establish the frequency–response characteristics of electrically elicited isotonic movements. Again, amplitude and phase were measured in averaged records of sixteen or thirty-two cycles, typical examples of which are shown in Fig. 4. Figure 5 shows Bode plots obtained in six different subjects. f_{180} values were in the

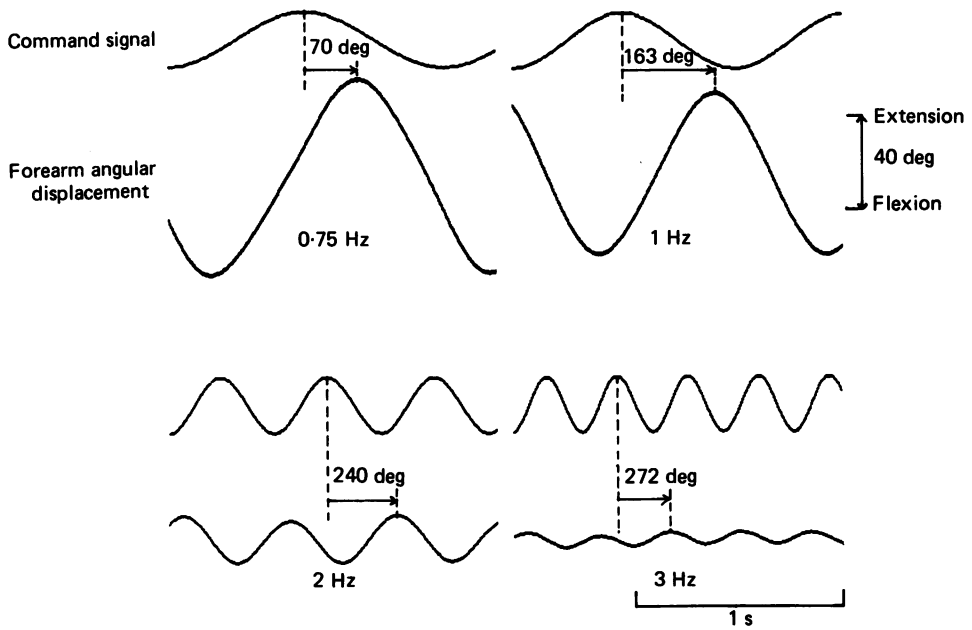

Fig. 4. Forearm displacement evoked by stimulus modulation at four different frequencies. Note that the responses decline rapidly in amplitude and develop large lags with increasing frequency.

range 1·5–3 Hz (mean phase curve: 1·6 Hz). The phase lags shown in Fig. 5 are not, of course, those of the complete loop, as further phase shifts are introduced by muscle receptors, nerve conduction and reflex transmission within the CNS. The results highlight the very low frequencies at which large phase lags develop purely as a result of the low-pass properties of the load-moving effector (in this case the muscles moving the inertial and viscoelastic load presented by the tissues of the forearm).

Closed-loop trials

The closed reflex arc was mimicked by routing the displacement signal through the spindle model ('Op. amp. array') and the 'Gain' and 'Inverter' amplifiers as shown in Fig. 1. The gain, initially set to zero, was then slowly increased, and in all subjects reached a characteristic and fairly reproducible threshold value above which instability occurred. Unlike the corresponding vibrator-evoked tremor (Prochazka & Trend, 1988), the electrically evoked oscillations tended to grow in amplitude unless the gain was critically adjusted to be just suprathreshold (Fig. 6). The mean frequency of the tremors, measured over the first two cycles, was 4·4 Hz (range

3·8–4·8 Hz). This was marginally higher than the mean frequency of 4·3 Hz at 10% maximal co-contraction in the vibration trials.

After the first few cycles of a growing tremor, the electrical stimuli became painful and the trial had to be terminated. In order to study the effects of delays within the closed loop, we felt it justified to introduce a limiting non-linearity into the forward

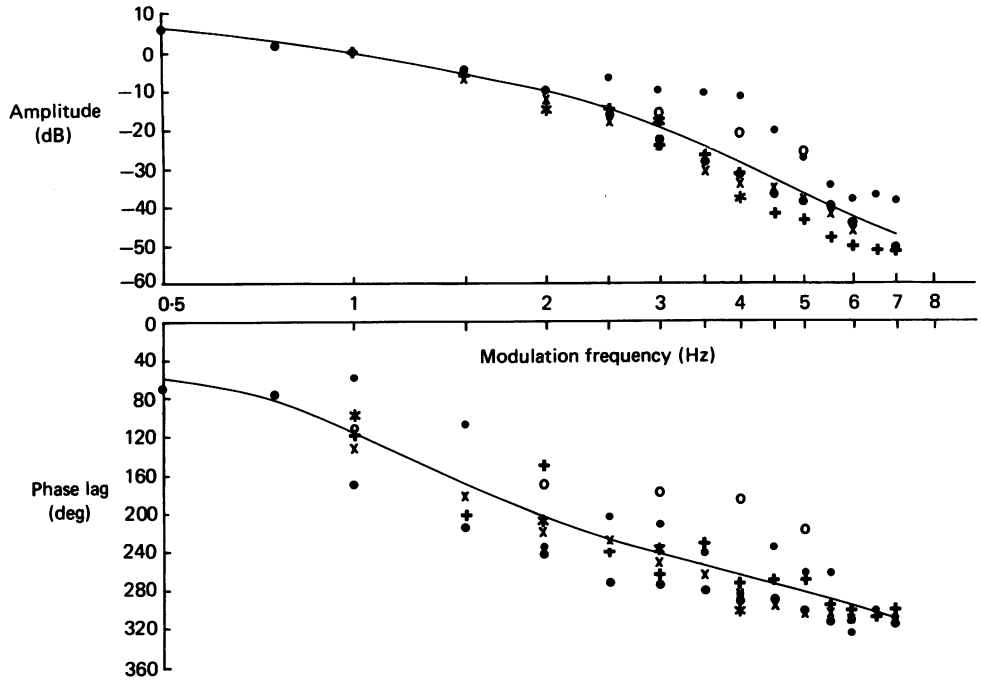

Fig. 5. Amplitude and phase plots of forearm movement *vs.* stimulus modulation frequency in six subjects. The smooth curves were drawn by eye through the means at each frequency (the geometric means in the case of gain). Frequencies at which phase lags first exceeded 180 deg (f_{180}) ranged from 1·5 to 4 Hz, with a mean of *ca.* 1·6 Hz.

pathway with the use of a logarithmic amplifier. Figure 6 (right column) shows the stable tremors which could be elicited with this modification. The frequencies of these tremors were 0·2–0·5 Hz lower than those observed at tremor onset but they were relatively insensitive to alterations in gain. The stability of these tremors allowed long segments of recording to be sampled for on-line Fourier analysis.

Figure 7 shows tremors elicited with closed-loop stimulation incorporating three delays: 20, 40 and 100 ms. These values were chosen as representing segmental, long-loop and pathologically increased conduction delays as described by various workers (reviewed by Marsden, Rothwell & Day, 1983; Lee, Murphy & Tatton, 1983). Two important effects of the increased delays are apparent in Fig. 7. First, the tremor amplitudes increased, and second, the frequencies decreased, with corresponding decreases in phase lag of movement on command signal. These effects are quantified in the Fourier spectra of Fig. 8.

A Fast Fourier Transform program supplied with the Cambridge Electronic Design 1401 interface was used to generate the plots shown in Fig. 8. The elbow

displacement signal, after low-pass filtering (40 dB/decade roll-off at 10 Hz) was sampled at 30 Hz for two consecutive 20 s epochs. The program produced an average of the spectra of the two epochs. Only the 0–5 Hz range of the spectra, containing the dominant peaks, are shown superimposed in Fig. 8. In this set of records, the tremor frequencies corresponding to 0, 20, 40 and 100 ms delays were 4·0, 3·6, 3·0 and 2·1 Hz

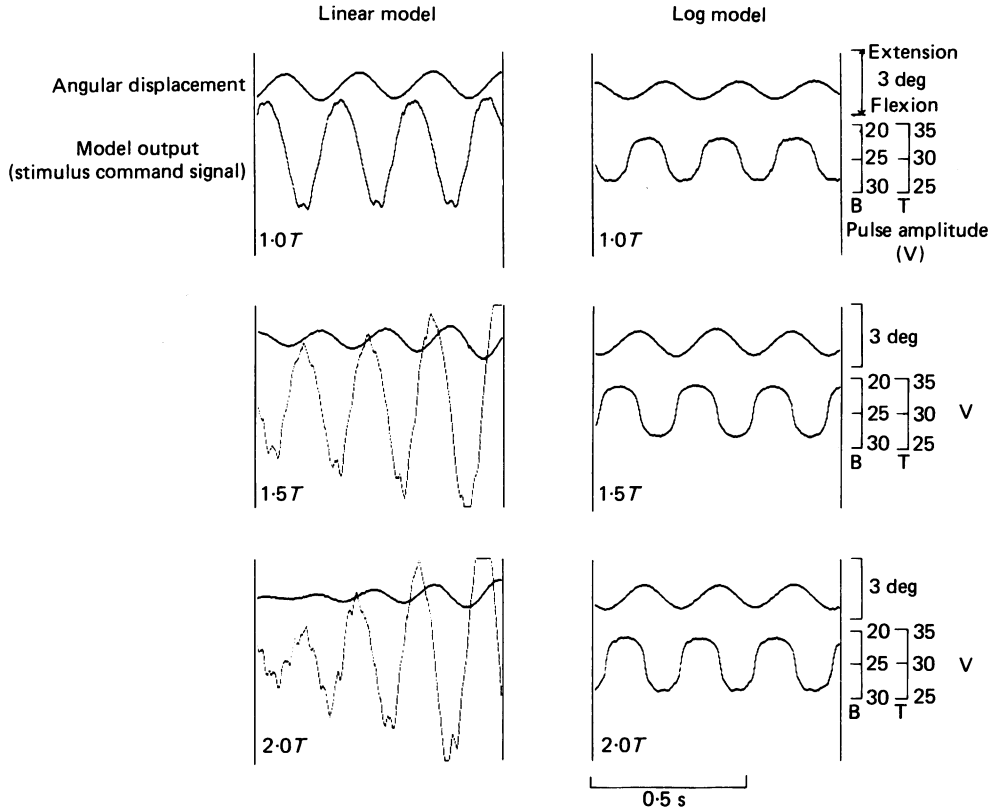

Fig. 6. Tremor in closed-loop trials. Left column, linear transfer function in spindle model. Right column, logarithmic element included in series with the linear transfer function. With the linear model, oscillation tended to grow rapidly with stimulus amplitude (expressed in terms of amplitude threshold for instability: 1·5 T and 2·0 T), though frequency at tremor onset was comparable. With the logarithmic model, oscillations were much less dependent on gain. B, biceps; T, triceps.

respectively. As will be seen in the Discussion, these frequencies are close to the values predicted by combining the open-loop phase characteristics of Fig. 5 with the calculated phase lags resulting from the delays at different frequencies. To a first approximation, the tremor periods were increased by twice the delay in each case.

DISCUSSION

In this study we mimicked hyperreflexia by 'replacing' part of the reflex arc with closed-loop electrical stimulation of muscles acting about the elbow joint. The

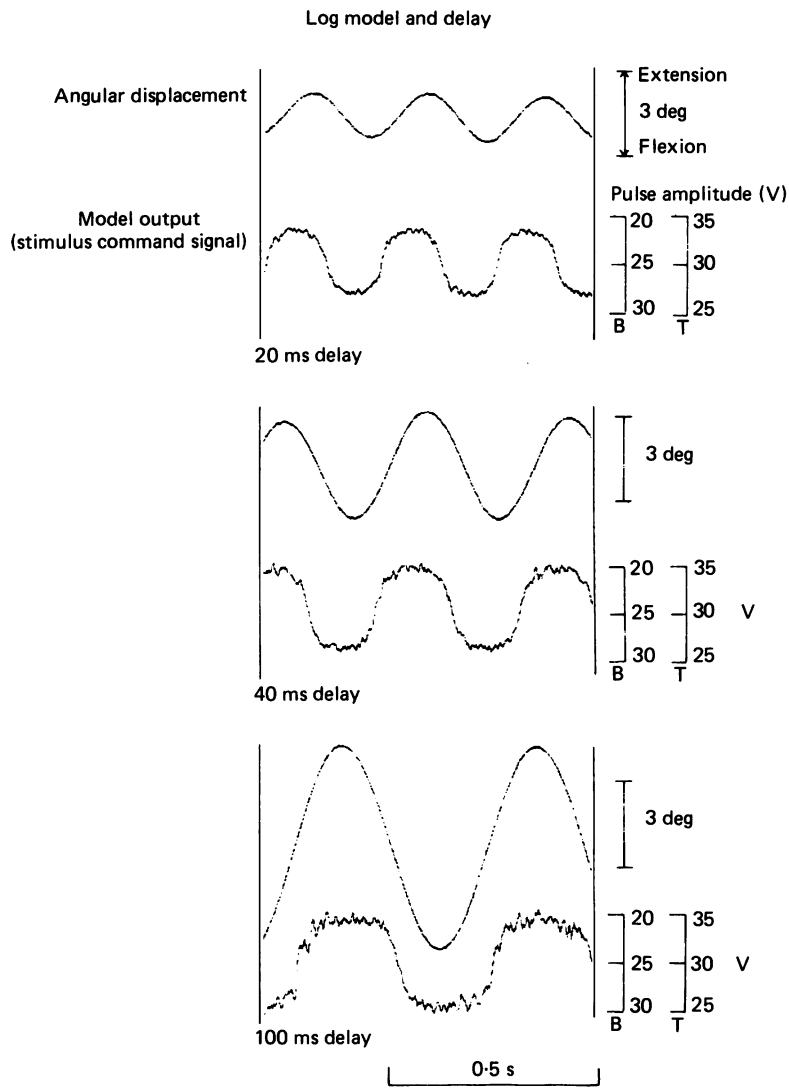

Fig. 7. Closed-loop oscillations observed with the logarithmic spindle model, with the inclusion of three delays (20, 40 and 100 ms) introduced into the loop via an analog delay line. The delays were chosen to mimic those due to conduction and central reflex processing. Note that the oscillations became progressively larger and of lower frequency.

approach was an extension of the feed-back-controlled vibration method used in the previous paper (Prochazka & Trend, 1988), and the results provide complementary support for the notion that stretch reflexes would be expected to assist low-frequency (3–8 Hz) tremor about the elbow.

Open-loop responses

The isometric frequency–response curves obtained with modulated electrical stimulation in our subjects showed similar low-pass characteristics to those described

for muscles in cats (Rosenthal *et al.* 1970; Mannard & Stein, 1973) and marginally higher roll-off frequencies than those in a comparable previous study in man (Aaron & Stein, 1976). Control models of the stretch reflex developed by Poppele & Terzuolo (1968) and Roberts, Rosenthal & Terzuolo (1971) used these isometric characteristics as a complete description of the forward pathway of the loop. However, reflexly the

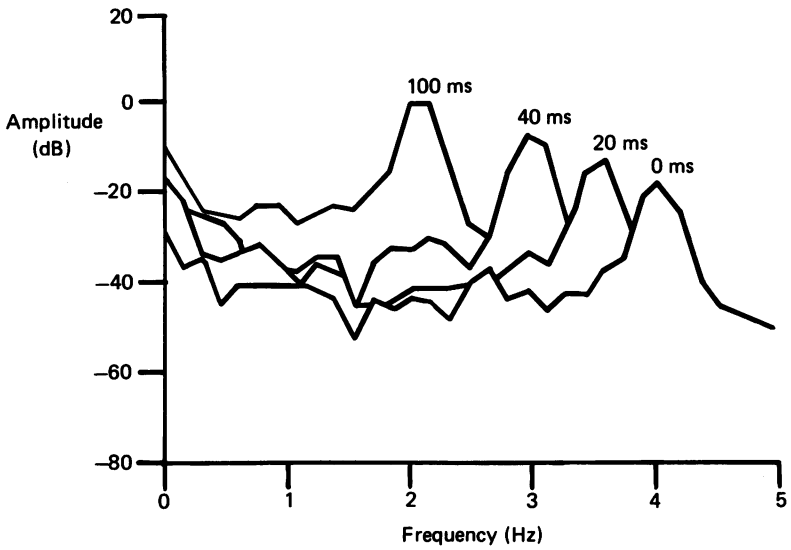

Fig. 8. Power spectra, obtained with a Fast Fourier Transform algorithm, of tremors evoked in the closed loop with delays included as in Fig. 7. Loop delays of 0, 20, 40 and 100 ms yielded spectral peaks at 4·0, 3·6, 3·0 and 2·1 Hz respectively.

most potent feed-back from the periphery usually comes from muscle length detectors, the spindle endings, rather than force detectors, the tendon organs (see later). Thus in order to be useful in analyses of stability, a description of the forward pathway should really include the transduction of muscle force into load displacement.

The data in Fig. 5 show that 180 deg phase lags of isotonic movement on command signal developed at frequencies as low as 1·5–3 Hz. This was lower than the 2·5–4·5 Hz range observed in vibration-evoked movements (previous paper: Prochazka & Trend, 1987), though higher than the 1 Hz value reported anecdotally for a similar open-loop electrical stimulation trial by Vodovnik *et al.* 1967. The discrepancy between the vibration and electrical stimulation trials could be due to a combination of the following factors.

(a) Our electrically produced movements might have had dynamic characteristics other than those resulting from the orderly, unsynchronized recruitment of motoneurones by the CNS. The isometric responses in our subjects were no slower than those in cat (Rosenthal *et al.* 1970), so it is unlikely that our particular method of stimulation was unrepresentative of electrical stimulation in general. However, electrical stimulation *per se* might produce a reversed order of motor unit recruitment, in that the larger α-axons (and therefore the larger, fast-twitch motor units) are excited first. Curiously, though this is demonstrable when stimulation is

applied through hook electrodes in contact with a thin, exposed motor nerve, percutaneous stimulation seems to recruit motor units randomly with respect to size and axonal conduction velocity (McComas, Fawcett, Campbell & Sica, 1971; Dengler, Stein & Thomas, 1988). Nevertheless, even a randomized recruitment order might boost the frequency response of muscle at low force levels, because of the increased participation of fast-twitch motor units. It is impossible to estimate the magnitude of this effect accurately. However, previous cat data give some idea of the maximal phase errors which might result from this type of distortion. Partridge (1965) compared electrically evoked tensions in soleus, which only has slow-twitch motor units, to those in gastrocnemius (mixed slow- and fast-twitch motor units). Soleus lagged gastrocnemius by 20 deg at 2 Hz and 40 deg at 4 Hz. Rosenthal *et al.* (1970) found that reflex-evoked tension in soleus lagged that in gastrocnemius by maximally 5 deg over the range 1–10 Hz. The use of electrical stimulation might therefore have led us to overestimate slightly the dynamic responsiveness of muscle to neural commands.

(b) Incomplete take-over of the spindle discharge by vibration, leading to overestimates of phase advance in the reflex-evoked movements. This possibility was discussed in the previous paper (Prochazka & Trend, 1988) and cannot be entirely excluded. To resolve this issue, one would ideally need to inject the command signal via the spindle afferents with absolute certainty as regards the spindle discharge. To our knowledge, there is no technique which would allow this in intact subjects.

(c) A genuine phase advance in the CNS contributing to the dynamics of the vibration-evoked movements. In the previous paper, the phase lags for the part of the loop comprising 'muscle–load + CNS + conduction path' were measured (Prochazka & Trend, 1988, Fig. 11, lower curve, reproduced, here: Fig. 9*C*). In the present paper, those for the 'muscle–load' alone were measured (Fig. 5, lower, mean curve reproduced in Fig. 9*A*). If factors (a) and (b) above are neglected, the phase differences between these two plots are therefore attributable to the 'conduction path + CNS'. At 1 Hz the difference is 40 deg, rising to 86 deg at 2·5 Hz, and declining to 0 deg at 6 Hz. The phase advances due to the CNS alone may be estimated by adding the corresponding lags due to the conduction delay. The minimal conduction delay in the reflex arc of biceps brachii is *ca.* 20 ms yielding phase lags of 7 deg at 1 Hz, 18 deg at 2·5 Hz and 43 deg at 6 Hz (eqn (1) below). The phase advances attributable to the CNS were therefore 47 deg at 1 Hz, 104 deg at 2·5 Hz and 43 deg at 6 Hz. Clearly if a larger delay had been chosen, larger estimates of CNS phase advance would have resulted.

In view of the various uncertainties outlined above, the absolute values of these estimates are of less interest than the qualitative conclusion that the CNS did seem to contribute appreciable phase advances in our experiments. In the decerebrate cat the responses of motoneurones to muscle stretch were nearly identical to those of group Ia afferents, suggesting that the spinal cord contributed little phase advance (Rosenthal *et al.* 1970; but cf. Westbury, 1970). In humans on the other hand, the phasic EMG responses at the onset of constant-frequency vibration are strongly indicative of a process akin to differentiation within the CNS (Matthews, 1984*b*), and this would certainly be more consistent with our findings.

Closed-loop behaviour

In terms of stability and the genesis of tremor, the important common feature of the open-loop responses, whether evoked by vibration or by electrical stimulation, was the low frequency at which 180 deg phase lags developed. When the loop was closed with the inclusion of spindle dynamics, the electrically stimulated arm

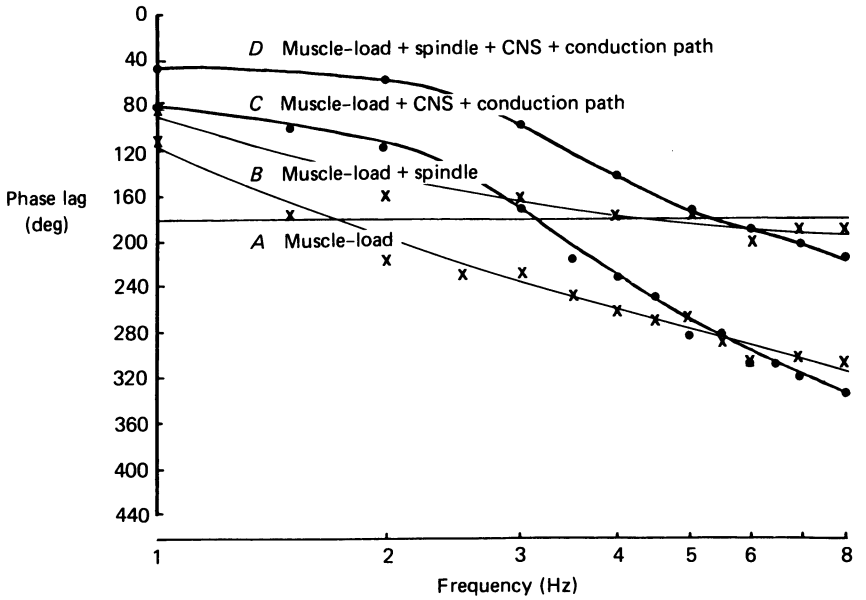

Fig. 9. Summary of open-loop phase data in this and the previous paper (Prochazka & Trend, 1988). Curve *A* is the mean phase curve of the muscle–load in response to electrical stimulation, reproduced from Fig. 5. Curve *B* shows the effect of adding the spindle phase advances from the spindle model (Poppele & Bowman, 1970). Curves *C* and *D* are the equivalent curves of the responses to vibration reproduced from the previous paper. Because the reflex arc was intact, *C* and *D* include the phase contributions of the CNS and the conduction path.

developed a growing tremor at a given threshold gain. The frequencies of the tremors we observed (mean 4·4 Hz) were comparable with those of the equivalent vibration-evoked tremors (Prochazka & Trend, 1988: 4·3 Hz), and this was consistent with the similar f_{180} values in the corresponding open-loop phase curves in Fig. 9*B* and *D*. (Note that curve *B* was obtained by adding to curve *A* the phase advances due to muscle spindle primary endings, derived from Poppele & Bowman's (1970) model.)

Closed-loop electrical stimulation of muscles acting about the elbow was first performed by Vodovnik *et al.* (1967). The aim at that time was to maximize loop gain for functional electrical stimulation purposes, and so the displacement feed-back was either unmodified or notch-filtered, neither of which were intended to model physiological transduction. With straightforward displacement feed-back, one subject was reported to have shown violent 1 Hz forearm oscillations. This is only

marginally lower than the frequency predicted from the f_{180} value of 1·6 Hz in Fig. 9 curve *A*.

Another interesting difference between our vibration and electrical stimulation experiments was the tendency for tremor to grow in the electrically evoked case, but to reach a steady-state amplitude of less than 1 deg peak-to-peak with vibration. We could mimic this latter behaviour in electrically evoked tremor by introducing an amplitude-limiting non-linearity into the loop. Such a non-linearity might in fact also have existed in the vibration trials, either as an artifact (spindles not following 1:1 at high vibration frequencies) or as a genuine transfer characteristic of the spinal cord. Muscle spindles show a marked drop in sensitivity as stretch amplitude increases (Matthews & Stein, 1969), and this could play a crucial role in limiting the amplitude of tremors seen in humans in health and disease.

Effects of delays

A delay in a feed-back loop has a destabilizing effect. If the delay is the only dynamic component in the loop, then at high gain oscillation develops at the frequency (f_{180}) at which the delay causes a 180 deg phase lag around the loop.

The phase lag ϕ due to a delay d (s) in a sinusoid of frequency f (Hz) is given by:

$$\phi = 360 \times d \times f \text{ deg.} \quad (1)$$

Thus the frequency f_{180} at which a delay d causes a 180 deg phase lag is

$$f_{180} = \frac{1}{2d}.$$

Delays of 20, 40 and 100 ms would cause 180 deg phase lags and oscillation at 25, 12·5 and 5 Hz respectively. Indeed Marsden (1978) reasoned that a reflex arc whose (only) dynamics comprised a conduction delay of about 50 ms would oscillate at 8–12 Hz, the frequency range of physiological tremor. The tacit assumption in this, that muscle–load properties were relatively unimportant in determining the tremor frequency, received some support from the models of Stein & Oguztöreli (1978). However, our results indicate that in the human forearm, the transfer characteristics of the muscle–load are at least as important as delays in the reflex pathway. Delays mimicking segmental (20 ms) short-latency (40 ms) and long-latency (100 ms) reflex transmission reduced the electrically evoked tremor frequencies from 4·0 Hz (due to muscle–load properties alone) to 3·6, 3·0 and 2·1 Hz respectively (Fig. 8).

An interesting point which emerges from the shape of the phase curves of Fig. 9 is that beyond 6 Hz further increases in phase lag seem likely. Extrapolating the data in Fig. 5, at 10 Hz the muscle–load could be expected to lag by some 340 deg. A 20 ms delay in the loop (segmental reflex) would add a further 72 deg. Subtracting the spindle afferent phase lead of 130 deg at 10 Hz (Poppele & Bowman, 1970), a net phase lag of just over 280 deg results. This lag is inconsistent with the loop supporting 8–12 Hz physiological or enhanced physiological tremors without unreasonable additional phase lead being ascribed either to the CNS pathway or to the spindle.

Internal phase advances

It is possible, however, that under certain circumstances f_{180} of the (open) reflex loop could shift into the 8–12 Hz range. First, during powerful co-contraction of agonists and antagonists, the participation of faster motor units, combined with increases in muscle stiffness, would most likely result in an increase in the bandwidth of the muscle–load system. In the previous paper, maximal co-contraction was found to increase tremor frequencies to nearly 8 Hz (Prochazka & Trend, 1988). A second possibility would be for large intramuscular (and therefore muscle spindle) phase advances to develop as a consequence of the in-series tendon absorbing a significant part of the muscle fibre displacement (Fellows & Rack, 1986, 1987). It now seems unlikely that this occurs in the forearm muscles of normal individuals (Amis, Prochazka, Short, Trend & Ward, 1987), though in theory it could happen if isolated members of a synergistic group of muscles were aberrantly activated (Fellows & Rack, 1987). One would then expect to see large internal movements of the muscle in the absence of, or out of phase with, joint displacement. A possible example of this is a rapid (16 Hz) tremor in large leg muscles recently reported in a neurological condition termed 'orthostatic tremor' (Thompson, Rothwell, Berardelli, Dick, Kachi & Marsden, 1986). Shivering tremor induced by cold in humans (e.g. 9·6 Hz, gastrocnemius: Eldred, Ott, Ishikawa & Stuart, 1966; 7–12 Hz, biceps brachii: Bawa, Matthews & Mekjavic, 1987) could also involve this mechanism on the qualitative grounds that the muscles sometimes appear to undulate under the skin, again with little associated limb movement.

Reflex contribution of tendon organs

In this study we have modelled stretch reflexes as though they were solely mediated by muscle spindle afferents, and we have ignored the possible reflex contribution of tendon organ afferents. The assessment of the strengths of tendon organ reflexes relative to those of muscle spindles is fraught with uncertainty. Monosynaptic reflex testing (Laporte & Lloyd, 1952) and intracellular recording in cat (Eccles, Eccles & Lundberg, 1957) originally showed that electrically evoked, presumed group Ib afferent volleys could sometimes exert powerful heteronymous and homonymous inhibition, but that this depended strongly upon the muscles involved, and upon descending and segmental facilitation (Hongo, Jankowska & Lundberg, 1969; Lundberg, Malmgren & Schomburg, 1978). H reflex (monosynaptic) testing has yielded broadly similar results in human leg muscles (Pierrot-Deseilligny, Morin, Bergego & Tankov, 1981; Pierrot-Deseilligny, Bergego & Katz, 1982; Fournier, Katz & Pierrot-Deseilligny, 1983). The doubtful selectivity of graded electrical stimulation (McIntyre, 1976), and the recent demonstration of Ia-mediated autogenetic inhibition (Fetz, Jankowska, Johannisson & Lipski, 1979) complicates the picture. Nevertheless, the existence of significant Ib-mediated reflexes, albeit smaller than those mediated by Ia afferents, is well established in experiments of this type in the cat (e.g. Harrison, Jankowska & Johannisson, 1983). In contrast, when less pulsatile variations in tendon organ input were evoked as test stimuli, reflex action relative to that of spindle input was low or negligible in the

decerebrate cat (Houk, Singer & Goldman, 1970; Jack & Roberts, 1978; Rymer & Hasan, 1980; Hoffer & Andreassen, 1981).

It is difficult to reconcile these conflicting results and to transfer them to our own experimental situation. In most electromyographic studies of human stretch reflexes, the contribution of tendon organ input has either been ignored, or inferred as being minimal (e.g. Gottlieb & Agarwal, 1980; Matthews, 1984*a*). A notable exception was the study of Newsom Davis & Sears (1970), in which a special analytical role was suggested for presumed tendon organ inhibition in the intercostal muscles. The time course of Ib activation in human tremor is likely to be of the sustained type evoked in the cat studies where tendon organ reflexes were minimal. Until more direct data become available on Ib contributions to reflexes in human arm muscles, we feel that it is reasonable to assume that there is a domination by Ia afferents of the reflex responses to muscle stretch in this situation, and that any alteration in the characteristics of Ia-mediated tremor would be minimal.

Pathological tremor

Rack & Ross (1986) recently showed that in patients with Parkinson's disease, stretch reflexes entrained by 3–5 Hz imposed mechanical oscillations assisted the movements and so could contribute to spontaneous Parkinsonian tremor. The authors speculated that the exaggerated long-latency (*ca.* 60 ms) stretch responses characteristic of Parkinsonian patients (Tatton & Lee, 1975) were involved. While our results are consistent with this conclusion, they also emphasize that in the 4–5 Hz range commonly quoted for Parkinsonian tremor (Marsden, 1984), the normal balance of short- and long-latency stretch reflexes seen in healthy individuals should be expected to contribute, and that it would be incorrect to assume that *only* exaggerated long-latency reflexes could support this low-frequency tremor. Regardless of whether imbalances of long- and short-latency reflexes were present, variations in co-contraction (rigidity) could act to 'tune' reflexes into and out of the frequency range of an otherwise centrally generated tremor (Rack, 1978).

Conclusions

In this and the previous study (Prochazka & Trend, 1988) we elicited instability in forearm control by 'taking over' part of the stretch reflex arc, and altering gains and delays within it. The main conclusion was that reflexes would tend to support tremor about the elbow at a lower frequency than expected. The properties of the muscles and their load (the forearm and hand) were important in setting the upper limit of tremor frequencies which could conceivably be supported by reflexes. Transmission delays had the expected effect of reducing these frequencies even further.

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